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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/509,608	06/19/2000	ALFRE WEBER	SCH1743	3126

7590

01/14/2002

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EXAMINER

KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
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1652

10

DATE MAILED: 01/14/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/509,608	WEBER ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 October 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>6</u> | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Application Status

1. A preliminary amendment was filed on June 19, 2000 (concurrent with the application), which amended Claims 4-8, 15-17, 21, 23, 25, and 26. Claims 1-26 are pending in the instant application and will be examined herein.

Priority

2. The instant application is granted the benefit of priority for International Application No. PCT/EP98/06134 filed on September 28, 1998 as requested in the declaration. The instant application also claims the benefit of German application 197 44 212.9 filed on September 30, 1997; however, no translation of said document is provided and this priority date cannot be granted. Thus, the priority date used for prior art in the instant Office action is September 28, 1998.

The Examiner notes that the requirements of national stage entry of the instant application had been completed on March 30, 2000, which is within 30 months of the earliest claimed priority date; the related international application includes both a search report and a preliminary examination report.

Information Disclosure Statement

3. The information disclosure statement filed on August 2, 2000 (Paper No. 6) has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

Drawings

4. The drawings are considered informal for the reasons detailed in the attached copy of PTO Form 948. Appropriate correction is required prior to allowance.

Objections to the Specification

5. The specification is objected to because on page 27, the description of Figure 4 contains German words. Foreign languages are not allowed in U.S. Patents. Appropriate correction is required.
6. The specification is objected to because an Abstract is missing. An abstract summarizing the teachings of the disclosure on a separate sheet of paper is required.

Objections to the Claims

7. Claim 1 is objected to for containing a typographical error. In line 9, the phrase "altered from" should be ---altered form---. Appropriate correction is required.
8. Claims 1 and 4 are objected to for containing an extraneous phrase. The last lines of both claims contain the limitation "and isolated" while the method step of purifying certainly isolates the products. The Examiner suggests deletion of this phrase to remove this redundancy.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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9. Claims 1-4, 7-10, and 26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term “intermediate products” as found in Claims 1 and 26 is confusing as to its metes and bounds. The starting reactant or all the reactions or both must be defined to particularly point out what is an ergosterol intermediate product and what is not. Appropriate clarification is required.

10. Claims 1, 4-6, and 8-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase “suitable genes of the ergosterol metabolic process” is unclear. The ergosterol metabolic process is not clearly defined, such as describing all the reactions and enzymes involved. Moreover, it is unclear what “suitable genes” are in this case. Appropriate clarification is required.

11. Claims 1-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The structure of Claim 1 is confusing since “a” and “b” are in the alternative while “c”-“f” must be included in the method. The Examiner suggests combining “a” and “b” into a single first step wherein the alternate form is chosen and designed and continuing the claim with the final four steps subsequently.

12. Claims 1-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

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the invention. The term “several” is indefinite because it implies more than 2, for example, but how many genes constitute “several” is wholly unclear.

13. Claims 1-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 1, line 5, the phrase “altered form” is wholly unclear. To what extent are the suitable genes to be altered? Moreover, specific genes are defined in dependent claims, and it is unclear if these are considered altered forms or not. Appropriate clarification is required.

14. Claims 1-10, 21-22, 25, and 26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claims 1, 21, 25 and 26, the phrase “fermentation into ergosterol” is unclear since no particular starting material is denoted and “into” implies from one product to another. The phrase should be rewritten as “fermentation of ergosterol” or some other suitable phrase. Appropriate correction is required.

15. Claims 2-3 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The structure of Claim 2 is *very* confusing using “2”, “a-i)”, and “i)” in addition to the variation between alternative elements and required elements. The Examiner suggests writing a design step as step a, then follow this with the subsequent required method steps c-f,

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then use a “wherein” phrase at the end of the claim to further define the design step. This “wherein” phrase should not contain confusing sub-headings.

16. Claims 2-3, 12-14, and 18-26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2-3, 12-14, 18-20 are replete with references to particular genes using the article “the”, which indicates a particular, singular product, while no single gene, for example, is pointed out. In Claim 2 for example, “**the** gene of HMG-CoA-reductase” (emphasis added) is unclear since more than one HMG-CoA reductase gene is known in the art. It is unclear which one gene is used in the claimed methods.

17. Claims 2-3 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The inappropriate use of parentheses is unclear. For example, in Claim 2, is only the “t-HMG” gene used in the claimed methods or can any HMG-CoA reductase gene be used? Moreover, is there a particular species from where these genes should be obtained?

18. Claims 9, 10, and 24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The pronoun “it” in each of these claims does not have proper antecedent basis. Thus, what “it” stands for is unclear.

19. Claim 11 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

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the invention. The antecedent basis of “a-i) in the process” is unclear since Claim 11 is independent.

20. Claims 12 and 13 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase “(altered variant of the HMG-1)” is unclear. Firstly, the language indicates a particular sequence that is not defined. Secondly, the parentheses are confusing for the reasons cited above for other parentheses. Thirdly, the particular alteration required is wholly unclear. Appropriate clarification of these matters is required.

21. Claims 12 and 13 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The references to figures in the instant claims are unclear. The Examiner suggests language like “as shown in” for clarity.

22. Claims 15-17, 21, 22, 25, and 26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of these claims is drawn to particular “uses” while none of these claims contain method steps. Moreover, the more appropriate preamble of such claims is, for example in Claim 15, “A method of producing ergosterol”.

23. Claims 18, 19, and 21-26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

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applicant regards as the invention. Claims 18 and 19 use the additional phrase "with the ..." when referring to additional genes in the vectors. It is unclear why this phrase is needed. Are all the genes equivalent in the vectors? Or does the "with" imply some sort of order or importance? Appropriate clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

24. Claims 1, 4-6, 8-10 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for processes of making ergosterol using *specifically* defined genes in host cells, does not reasonably provide enablement for processes of making ergosterol using *any* genes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The breadth of the instant claims cannot be achieved by one of skill in the art without undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized in *re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The Court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is

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needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The specification contains a single example of using more than one gene involved in ergosterol biosynthesis, Example 3 using t-*HMG* and *SAT1*. The specification contains no examples of using genes involved in the breakdown of ergosterol (also a metabolic process). The lack of definition of which genes are used in the methods (see second paragraph rejection above) widens the breadth of unpredictability using **any** gene to make ergosterol. Sterol biosynthesis is governed by numerous, complicated pathways using gene products and regulatory factors (see EP 0 486 290 A2 (IDS reference), page 4, lines 19-30). The ability to predict the effect (i.e., the ability to still produce ergosterol) is very low in such a broad genus.

25. Claims 1, 4-6, 8-10 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to methods of making ergosterol using genes that are defined only by function, i.e., involvement in ergosterol metabolic processes.

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The Court of Appeals for the Federal Circuit has recently held that a “written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as be structure, formula [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

The instant specification describes the genes to be used in the claimed methods by virtue of function alone. No structures, other than specific species of genes, are described. No relation between the structure of the species and function is described. Thus, one of skill in the art would be required to predict new genes for use in the claimed methods based solely on their function, or the function of their encoded proteins. Such methods would not be predictably considering the minimal structural information provided in the specification.

26. Claims 7 and 10-17 are rejected under 35 U.S.C. § 112, first paragraph, enabling deposit, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. To practice the instant methods or to make the claimed products,

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one of skill in the art is required to use YepH2, YDpUHK3, and pADL-SAT1 plasmids or AH22 cells. The instant specification contains no deposit information concerning these plasmids and/or cells. To enable the instant claims by enabling the deposit of YepH2, YDpUHK3, and pADL-SAT1 plasmids or AH22 cells, the following items are required: (1) the accession number assigned by the depository, (2) the date of deposit, (3) a brief description of the deposit, (4) the name and full address of the depository (37 C.F.R. § 1.801 - 1.809) (those which are in bold have not been fulfilled by the instant specification), and (5) the record must also contain a statement certifying that all restrictions on accessibility to said deposit be irrevocably removed by Applicant upon the granting of the patent (see M.P.E.P. § 2404.01); this statement may be certified by Applicants or Applicants' representative.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

27. Claims 1, 5, 8, and 9 are rejected under 35 U.S.C. § 102(b) as being anticipated by Saunders *et al.* (EP 0 486 290 A2 – IDS reference). The instant claims are drawn to methods of making ergosterol intermediate products, particularly squalene, in *S. cerevisiae* using more than one ergosterol gene on plasmids transformed into the yeast, fermentation, extraction, and purification of squalene using column chromatography.

Saunders *et al.* teach methods of making squalene using *S. cerevisiae* transformed with a gene encoding HMG-CoA reductase activity (see Abstract). Saunders *et al.* further teach using mutant yeast host cells, for the transformation above, having been previously transformed with mutant *erg3*, *erg5*, *erg6*, or a combination thereof (see page 11, lines 41-60). Saunders *et al.* also teach fermentation, extraction, and purification of squalene using column chromatography (see page 13).

Conclusion

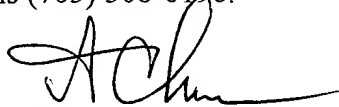
28. Claims 1-26 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK
January 10, 2002


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